REMARKS

Claims 1, 2, and 4-14 were pending in the application upon issuance of the Final Office Action date May 23, 2007 (Paper No. 20070514). According to the foregoing amendments, claims 1, 2, 4-7 and 9 have been cancelled, claims 8 and 10-13 have been amended, and new claims 18-26 have been added. Following entry of this amendment, claims 8 and 10-26 will be pending in the instant application.

Support for the claim amendments can be found throughout the specification and in the claims as originally filed. Specifically, support for the amendments to claims 8, 10, and 13 can be found in the specification at least at page 106, line 26 to page 107, line 13; page 125, line 34; and page 136, line 8. Support for new claims 18-26 can be found in the specification at least at page 89, lines 24-27 and at page 100, lines 9-26.

The specification has been amended to update the status of referenced non-provisional U.S. Patent Applications. In addition, the specification has been amended to replace the notation "Attorney Docket No." with the serial numbers of referenced U.S. Patent Applications.

No new matter has been added by the foregoing amendments. Applicants request that the amendments to the claims and specification be entered. The foregoing claim amendments should in no way be construed as acquiescence to any of the Examiner's rejections and were made solely to expedite prosecution of the present application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Interview

Applicants wish to thank the Examiner for the courtesy of a personal interview on March 6, 2008 conducted at the USPTO with Applicants' attorneys Elizabeth Hanley and Cristin Cowles. During the interview, amendments to the claims were discussed. In particular, it was pointed out that the amended claims in the instant Amendment and Response were not rejected under 35 USC § 112, 1st paragraph in the final Office Action dated May 23, 2007 with respect to CDR sequences. It was also discussed that the limitations of the amended claims (submitted herewith) were not taught or suggested by the combination of references cited under 35 USC § 103.

Objection to the Specification

The Examiner has indicated that the specification should be updated to include the current status of non-provisional U.S. Patent Applications referenced therein. The status of the non-provisional U.S. Patent Applications has been updated as requested. The specification has additionally been amended to replace the notation "Attorney Docket No." with the serial numbers of referenced U.S. Patent Applications. The title of the application will be amended in accordance with the Examiner's recommendation upon allowance of the claims.

Rejection of Claims 5, 9 and 12 Under 35 U.S.C. § 112, first paragraph:

The rejection of claims 5, 9 and 12 under 35 U.S.C. § 112, first paragraph was maintained on the ground that the specification "does not reasonably provide enablement for a method ... as broadly encompassed by the claims" as previously amended. In particular, the Office Action asserts that the teachings and exemplification are limited to antibodies and antigen-binding fragments thereof that "comprise all six CDRs, three from the heavy chain and three from the light chain of human anti-human TNFα antibody D2E7" and therefore the specification does not provide support for antibodies and antigen-binding fragments thereof that "only comprise the CDR3 domains of D2E7" with a specific K_{off} dissociation rate.

Applicants respectfully traverse this rejection. Applicants assert that not all of the CDRs of the antigen binding site may be necessary (or even utilized) in binding a specific antigen, and that functional antibody fragments comprising fewer than all 6 CDRs are well known by practitioners skilled in the art. Notwithstanding the foregoing, and in the interest of expediting examination, Applicants have canceled claims 5 and 9, thereby rendering rejection of these claims moot. Applicants submit that the cancellation of claims 5 and 9 in no way is acquiescence to the Examiner's rejection. Applicants preserve the right to pursue the subject matter of claims 5 and 9 in a future continuation or divisional application.

Claim 12 has been amended to depend from claims 8 and 9. In light of the cancellation of claims 2, 5, and 9 and the amendment of claim 12, Applicants respectfully submit the rejection is rendered moot.

Rejection of Claims 1-2 and 4-14 under 35 U.S.C. § 103(a)

The rejections of the pending claims, 1-2 and 4-14, as being *prima facie* obvious over

(1) Oh *et al.* (Journal of the American Academy of Dermatology, 42(5):829-830, 2000) in view of Salfeld et al. (WO 97/29131) or (2) Oh *et al.* in view of Salfeld *et al.* (US Patent 6,509.015) were maintained (Applicants note that claims 1, 2, 4-7 and 9 have been canceled, thereby rendering rejection of these claims moot). Specifically, the Office Action stated that

> In this case, one of ordinary skill in the art would have been motivated to modify the method of Oh et al. using the human anti-human TNFa antibodies and antigen-binding fragments thereof of Salfeld et al. (i.e., identical to the claimed antibodies) in order to avoid any unwanted immune reaction in human patients due to the presence of murine sequences in the chimeric anti-TNFa antibody of Oh et al. The strongest rationale for combining the references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. (Office Action at page 10)

Applicants respectfully traverse this rejection.

Amended claims 8 and 10-13 each describe methods comprising *biweekly, subcutaneous administration of a unit dosage form comprising about 10-150 mg* of a human anti-TNFa antibody, or an antigen binding fragment thereof. In addition, new claims 18-21 describe methods comprising *biweekly, subcutaneous administration of a unit dosage form comprising about 20-80 mg* of a human anti-TNFa antibody, or an antigen binding fragment thereof, and new claims 22-25 require *biweekly, subcutaneous administration of a unit dosage form comprising about 40 mg* of a human anti-TNFa antibody, or an antigen binding fragment thereof.

"To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." (See MPEP § 2143).

Oh *et al.*, the primary reference relied upon to support the rejection, describes a patient who received a *single intravenous infusion of 5 mg/kg* of a chimeric TNFα antibody, *i.e.* infliximab. Oh *et al.* suggests that the patient showed an improvement in the appearance of their psoriasis 4 weeks after the infusion. This reference further mentions that the patient's improvement was gradually lost (*i.e.*, the patient's PASI scores returned to baseline), and that

a second intravenous infusion of 5 mg/kg of the antibody 16 weeks after the first infusion resulted in a similar course of clinical improvement of the patient's psoriasis. Oh *et al.* fail to teach or suggest a method of treating psoriasis comprising *biweekly, subcutaneous administration* of a *unit dosage form comprising 10-150 mg* of a TNFα antibody.

Moreover, the substitution of the human TNFα antibody (D2E7) taught by Salfeld *et al.* in the method of treating psoriasis taught by Oh *et al.* for the purported benefit of avoiding any unwanted immune reaction still fails to render the presently claimed invention *prima facie* obvious. Neither reference alone or in combination expressly or impliedly teaches a course of treatment for psoriasis involving *biweekly, subcutaneous administration* of a *unit dosage form comprising 10-150 mg* of a human TNFα antibody. In view of the required elements of amended claims 8, 10 and 11 and claims depending therefrom, Applicants respectfully submit that Salfeld *et al.* fails to make up for the deficiencies of Oh *et al.* Accordingly, Applicants respectfully request that the rejection of the pending claims under 35 U.S.C. § 103 be reconsidered and withdrawn.

Rejection of Claims 1-2 and 4-14 On Grounds of Non-Statutory Obviousness-Type Double Patenting

The rejection of claims 1-2 and 4-14 as being unpatentable on the ground of nonstatutory obviousness-type double patenting over claims 1-7, 16, 36-39, 49 and 69-70 of US Patent 6,509,015 B1 (Salfeld *et al.*) in view of Oh *et al.* was maintained. The Examiner suggests that claims 1-2 and 4-14 are not patentably distinct from claims 1-7, 16, 36-39, 49 and 69-70 of US Patent 6,509,015 B1 (Salfeld *et al.*) in view of Oh *et al.* because "one of ordinary skill in the art would have been motivated and had a reasonable expectation of success at the time the invention was made to modify the therapeutic method of claims 1-7, 16, 36-39, 49 and 69-70 of US Patent 6,509,015 B1 for the treatment of psoriasis in a human patient because Oh *et al.* teach the administration of an anti-TNFa antibody effectively treats prosiasis in a human patient."

Applicants note that the pending claims all require *biweekly, subcutaneous administration* of an anti-TNFa antibody, or antigen binding portion thereof, as a unit dosage form. The Examiner relies on Oh *et al.* to make up for the deficiencies of claims 1-7, 36-39 and 69 of Salfeld *et al.* Applicants respectfully submit that in view of the fact that Oh *et al.* do not teach or suggest all of the limitations of the claims, as described above, Oh *et al.* fail to

make up for the deficiencies of Salfeld et al. As such, Applicants respectfully request that the rejection of claims 1-2 and 4-14 on the ground of nonstatutory obviousness-type double patenting be withdrawn.

Provisional Rejection of Claims 1-2 and 4-14 On Grounds of Non-Statutory Obviousness-Type Double Patenting

The provisional rejection of claims 1-2 and 4-14 as being unpatentable on the ground of nonstatutory obviousness-type double patenting over claims 1-23 and 73-84 of copending Application No. 10/163,657 in view of Oh *et al.*; the provisional rejection of claims 1-2 and 4-14 as being unpatentable on the ground of nonstatutory obviousness-type double patenting over claim 15 of copending Application No. 11/233252 in view of Oh *et al.* and Salfeld *et al.* (WO 97/29131); and the provisional rejection of claims 1-2 and 4-14 as being unpatentable on the ground of nonstatutory obviousness-type double patenting over claim 15 of copending Application No. 11/104117 in view of Oh *et al.* and Salfeld *et al.* (WO 97/29131) were maintained in the Final Office Action.

Applicants note that these rejections are provisional in nature and respectfully submit that they will be further addressed when appropriate, *i.e.*, when the nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the later-filed application (MPEP § 804 I.B.).

SUMMARY

In view of the foregoing, Applicants believe that the application is now in condition for allowance. If a telephone conversation with Applicant's Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicant's Attorney at (617) 227-7400.

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Respectfully submitted,

By _____

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